REMARKS/ARGUMENT

SUMMARY OF THE PRESENT AMENDMENT

In accordance with Rule 173(g), all of the amendments herein are relative to the issued patent -- not relative to the text that existed prior to the present amendment. Amendments other than those being presented for the first time herein were previously discussed in prior submissions. In order to simplify the proceedings, all method claims are canceled herein, without prejudice to their being pursued in a continuing application hereof. Likewise, claims 15 and 18 have also been canceled to simplify the proceedings. Claims 24 and 27, which were previously dependent from claim 15 have been amended to depend instead from claim 13. All other claims previously dependent from claim 15 (directly or indirectly) have been canceled. All cancellations are without prejudice to the involved subject matter being pursued in a continuing application hereof.

As requested by Mr. Celsa at the November 12, 2008 interview described *infra*, the preamble of all remaining independent claims has been amended to recite that the pharmaceutical compositions are "for nasal administration." For reasons discussed in more detail *infra,* applicant views this as a clarification of previously-existing claim language, and not as a narrowing amendment. Applicant believes that in the context of the present specification "pharmaceutical compositions" necessarily refer to "nasal" pharmaceuticals even where "nasal" is not expressly stated. Following this amendment to claim 13, the previously-existing language near the end of claim 13 requiring that the pharmaceutical composition be "suitable for nasal administration" was deleted to avoid redundancy. If the Examiner disagrees that this phrase is now redundant, Applicant is willing to reinsert that language.

Finally, the prior specification amendments that raised "new matter" objections at the interview have been deleted. Minor specification amendments that are clearly supported

by the original text (e.g correction of clear grammatical or typographical errors) have been retained. Support for the amendment to Column 3, lines 15-20 is at original claim 15. That amendment was previously requested by the Examiner. However, Applicant is also willing to remove any of the remaining specification amendments that the Examiner believes continue to present "new matter" issues.

SUMMARY OF INTERVIEW SUBSTANCE UNDER M.P.E.P. § 713.04

A personal interview was held at the United States Patent and Trademark Office (PTO) on November 12, 2008. In attendance were Examiner Mina Haghighatian, S.P.E Johann Richter, Quality Review Board Member Bennett Celsa, inventor William Stern and Applicant's representative, William Gray.

Applicant agrees with the summary set forth by Examiner Haghighatian in her interview summary provided to applicants by facsimile on November 12, 2008.

Mr. Celsa requested that Applicant remove certain specification amendments that were viewed as "new matter." Without conceding the "new matter" issue, and in order to advance the prosecution, Applicant agreed to remove the specification language in question. Applicant pointed out that the revised data set forth in the prior specification amendments (and in several of Dr. Stern's prior Declarations) were submitted in accordance with Applicant's duty of disclosure, and were not required to establish patentability of the claims, or to establish unexpected results. Applicant noted that the same conclusions flow from both the original and revised data, *inter alia*, that unexpected advantageous results arise from using the narrowly-defined citrate concentrations recited in the instant claims. See the more extensive discussion of the conclusions to be drawn from Tables 1 and 3, *infra*.

Regarding Applicant's duty of disclosure, while the specification is being amended at the request of the PTO to reflect the original unrevised data, the revised data remain available to the PTO, and to the public, by reference, *inter alia*, to the amendment filed August 13, 2008 and to the Second, Third and Fourth Declarations of inventor William Stern, previously filed.

Mr. Celsa also requested that the preamble of the independent claims be amended to more expressly require that the pharmaceutical compositions of the invention be for nasal administration. Applicant noted that, in the context of the present patent application, Applicant already interpreted and intended that the claimed "pharmaceutical compositions" be pharmaceutical products for nasal administration. In the present amendment, Applicant amends the claims to insert the language requested by Mr. Celsa. Applicant believes that this language merely makes express a limitation that was at least implied in the prior claim language. Hence, Applicant does not view this as a narrowing amendment.

The Chiodini reference, particularly example 19 thereof, was discussed in connection with the most recent prior art rejection. Applicant noted that Chiodini neither discloses nor suggests the combination of narrow citrate range and pH range set forth in claim 13. Additionally, applicant believes that Chiodini uses citrate only as a buffer - - not for applicant's use of citrate to affect bioavailability and shelf stability. Dr. Stern has further analyzed the Chiodini reference in a new FIFTH DECLARATION OF INVENTOR WILLIAM STERN UNDER 37 C.F.R. §1.132 (Stern-V) that is submitted herewith. Stern-V further distinguishes Chiodini, and in more detail, as discussed *infra*. It was also noted at the interview that Chiodini example 19 utilizes elcatonin whereas Applicant's claim 19 is limited to salmon calcitonin.

Applicant noted that the other prior art cited in the most recent written office action also fails to disclose or suggest the presently-claimed pharmaceutical compositions.

Mr. Celsa questioned whether claims 22 and 23 might be overly broad, and whether the tonicity of any of the Chiodini examples might place those examples within the scope of claim 15. While Applicant believes that claims 15, 22, and 23 are directed to patentable subject matter, Applicant has not looked into those issues in connection with the present amendment because those issues are now moot in view of the cancellation of claims 15, 22 and 23 (without prejudice to their being pursued in a continuing application).

GENERAL REMARKS ON THE CHIODINI REFERENCE AND NEW MATTER ISSUES

The same conclusion of non-obvious unexpected results can be derived from both the original and revised versions of Tables 1 and 3

As noted in paragraphs 2-4 of the accompanying Stern Declaration (Stern V), Dr. Stern has reviewed the data set forth in Tables 1 and 3 of original U.S. Patent No. 6,440,392 (hereinafter "Original Tables 1 and 3"), as well as the revised data set forth in prior amendments to Tables 1 and 3 that have been made during the reissue proceedings (hereinafter "Revised Tables 1 and 3"). The present amendment replaces the Revised Tables 1 and 3 with Original Tables 1 and 3. Dr. Stern states that the same conclusions may be drawn from both the Original and Revised data, and hence that the present amendment does not adversely affect the showing of unexpected results that applicant has previously made.

Referring to Table 1, both Original and Revised Table 1 show a significant increase in the bioavailability of the salmon calcitonin active agent when citrate concentration is increased from 0 to 10 mM. (As used herein, "citrate" means the combined concentration of citric acid and citric acid salt regardless of the acid/salt ratio). Both Original and Revised Table 1 show further improvements in bioavailability as citrate concentrations are further increased. In both Original and Revised Table 1, the foregoing effect on bioavailability is solely a function of citrate concentration because all other parameters

are held constant as citrate concentration is varied. This is an unexpected citrate effect that is neither disclosed nor suggested by the cited prior art. (See Stern-V, paragraph 5).

Referring to Table 3, both Original and Revised Table 3 show an unexpected reduction in shelf stability of salmon calcitonin formulations at the higher citrate concentrations reported therein. In both Original and Revised Table 3, the foregoing effect on shelf stability is solely a function of citrate concentration because all other parameters are held constant as citrate concentration is varied. This is an unexpected citrate effect that is neither disclosed nor suggested by the cited prior art. (See Stern-V, paragraph 6).

For the reasons stated in Stern-V, paragraphs 5 and 6, Tables 1 and 3 together establish unexpected results, on the combination of bioavailability and shelf stability, that arise from utilizing the citrate concentrations set forth in the present claims. This is equally true regardless of whether Original or Revised Tables 1 and 3 are being considered. Thus, the present amendment returning Tables 1 and 3 to their original condition has no effect on the showing of unexpected results that Applicant has previously made. (See Stern-V, paragraph 7).

In paragraph 8 of the Stern-V declaration, Dr. Stern also concludes that none of the other original specification language being reinserted herewith changes his foregoing opinion regarding the teachings of specification Tables 1 and 3 (Original or Revised). Thus, both with and without the accompanying amendment, the specification enables a person of ordinary skill in the art to make and use the invention as presently claimed. Moreover, the specification, both with and without the accompanying amendment, establish unexpected results for the claimed compositions.

The Chiodini reference neither discloses nor suggests the claimed invention.

Chiodini Example 19, discussed during the interview of this application on November 12, 2008, has a pH of 6 that is well outside of the pH range recited in present claim 13 (i.e. 3.5-3.9). A pH of 6 would be too high for adequate shelf stability in the claimed nasal pharmaceutical compositions (Stern-V, paragraph 9). For reasons stated *infra*, the very broad pH ranges stated elsewhere in Chiodini do not disclose or suggest to a person of ordinary skill in the art that Chiodini Example 19 should be modified in a manner that results in a formulation whose pH and citrate concentration are simultaneously within the ranges recited in claim 13 of the present application. Specifically, Chiodini Example 19 uses a citric acid/sodium citrate buffering solution to adjust pH. If Chiodini were to add enough additional citric acid to reduce the pH of the Example 19 solution to 3.9 (the top pH permitted by claim 13 of the present application), at least 443 mg of additional citric acid would be required, and even more if Chiodini has added sodium hydroxide as shown on the final line of Example 19 (Stern-V, paragraph 10). The addition of the above-noted 443 mg of citric acid would bring the total citrate concentration of Chiodini Example 19 to 41 mM, well above the maximum citrate level permitted by the present claims (Stern-V, paragraph 10). As shown in Tables 1 and 3 of the application (both Original Tables 1 and 3 and Revised Tables 1 and 3), the claimed citrate ranges are critical to achieving both good shelf stability and good bioavailability. Chiodini, in using citrate only as a buffer, did not disclose or suggest the effect Applicant has shown citrate to have on these parameters. Thus, Chiodini did not disclose or suggest any reason to limit citrate concentration while adjusting pH (Stern-V, paragraph 10). Moreover, the final line of Chiodini example 19 suggests the need to adjust pH upward away from Applicant's claimed pH range - - rather than downward - - by adding sodium hydroxide if pH were otherwise below 6.

Chiodini views citrates only as buffers (not as agents that affect bioavailability and shelf stability as taught in the present patent application). See Chiodini, Column 6, lines 13-25,

where citrates are discussed for their buffering capability, and where Chiodini assumes that they are interchangeable with other non-citrate buffering systems. Indeed, the Chiodini reference does not report any data indicating that any of the formulations in Chiodini example 19 were tested for either bioavailability or shelf stability. (See Stern-V, paragraph 12).

For all of the foregoing reasons, it is urged that the claimed invention is not obvious over Chiodini.

SUBMISSION OF REISSUE INVENTOR'S DECLARATION

Applicant encloses another Supplemental Declaration for Reissue Patent Application to Correct "Errors" Statement (37 C.F.R. 1.175).

CONCLUSION

It is believed that the application is now in condition for allowance. Issuance of a notice of allowance is solicited. The examiner is invited to call the undersigned to resolve any other issues that, in her opinion, are not adequately addressed by the present submission.

THIS CORRESPONDENCE IS BEING SUBMITTED ELECTRONICALLY THROUGH THE PATENT AND TRADEMARK OFFICE EFS FILING SYSTEM ON November 17, 2008.

WOG:db

Respectfully submitted,

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APPENDIX A

Claim Number (Status)	Nature of Change/Recitation	Supporting Text in Original Patent
1-12 (canceled)	n/a	n/a
13 (pending)	citric acid concentration; rewritten in independent form; "and/or" changed to Markush format; Preamble recites for nasal administration	Table 1; Table 3; original claim 13;
14 (pending)	claim dependency only	original claim 14
15 (canceled)	n/a	n/a
16 (pending)	claim dependency only	original claim 16
17 (pending)	claim dependency only	original claim 17
18 (canceled)	n/a	n/a
19 (pending)	typographical error "MRC"; preamble recites for nasal administration	original claim 19; Table 1
20 (canceled)	n/a	n/a
21 (canceled)	n/a	n/a
22 (canceled)	n/a	n/a
23 (canceled)	n/a	n/a
24 (pending)	citric acid concentration	Claim 19
25 (canceled)	n/a	n/a
26 (canceled)	n/a	n/a
27 (pending)	aqueous saline	col. 3, line 2
28 (canceled)	n/a	n/a
29 (canceled)	n/a	n/a
30 (canceled)	n/a	n/a

Claim Number (Status)	Nature of Change/Recitation	Supporting Text in Original Patent
31 (pending)	aqueous saline; osmotic pressure	col. 3, line 2; col. 3, lines 16-18
32 (pending)	salmon calcitonin	examples 1, 2 and 3
33 (canceled)	n/a	n/a
34 (pending)	method of nasal administration	original claim 20; col. 3, lines 43-56
35 (canceled)	n/a	n/a
36 (canceled)	n/a	n/a
37 (canceled)	n/a	n/a
38 (canceled)	n/a	n/a
39 (canceled)	n/a	n/a
40 (canceled)	n/a	n/a
41 (canceled)	n/a	n/a
42 (canceled)	n/a	n/a
43 (canceled)	n/a	n/a
44 (canceled)	n/a	n/a
45 (pending)	preservatives	original claim 17